

BIOMATERIALS

UDC 666.11.002.69:61

POROSITY AND SOLUBILITY OF BIOACTIVE CALCIUM-PHOSPHATE GLASS CERAMIC MATERIALS FOR BONE ENDOPROSTHESIS REPLACEMENT

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Translated from *Steklo i Keramika*, No. 5, pp. 40 – 45, May, 2012.

Questions concerning the solubility of glass ceramic materials based on calcium-phosphate glass in water and solutions simulating the physiological medium of a living organism are examined. The relation between the level, character and size of pores in a material and its solubility is determined. Recommendations for using the new materials in medical practice are made.

Key words: biomaterials, glass ceramic materials, porosity, solubility, bone endoprosthesis replacement.

Twenty-first century medicine is close to solving the problems of restoring damaged or dead organs using the body's own resources. In the 1970s, together with materials conventionally used to replace damaged bone tissues (metals, polymers, ceramics, and graphite), materials of new type appeared, so-called biomaterials. They did not become encapsulated by connective tissue when coming into contact with bone, adhered to the bone and in time formed a single implant – bone fragment [1]. The avalanche-like growth of the number of publications on the development, optimization and technology of these materials points to the unabated interest in them (Fig. 1).

The problem today is to develop functionally oriented biomaterials that secure “social” behavior of surrounding cells and organotypic restoration of damaged tissues [2]. For treating bone trauma and diseases this means that not only is the implant material compatible with the adjoining bone tissue but it also triggers a mechanism for replacing the bone tissue, functioning both as a matrix and building material.

Natural bone tissue is a porous composite, where the carbonate-hydroxyapatite (CHA) is the matrix and the fillers are collagen fiber, blood vessels and other biochemical components. The pore structure of the matrix is nonuniform — the surface cortical layer is characterized by low porosity (to

10%) with pore size to 200 μm ; the interior capillary layer is highly porous with pore space volume to 90% and pore size to 1000 μm . The reconstruction of such a structure in an endoprosthesis or implant is a quite complicated technological problem, but it can be simplified by creating materials with two-level porosity and sufficiently high resorbability in the natural physiological medium.

The currently known bioactive matrix-materials compositions are limited by to calcium-phosphate and silicate systems. This becomes understandable if the processes that promote joining of the materials with bone are examined.

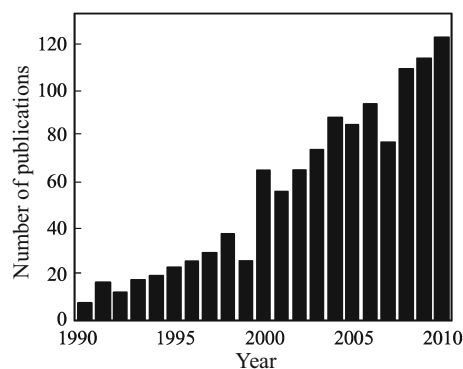


Fig. 1. Growth of the number of publications on materials for bone endoprosthesis replacement from 1990 to 2010 [1].

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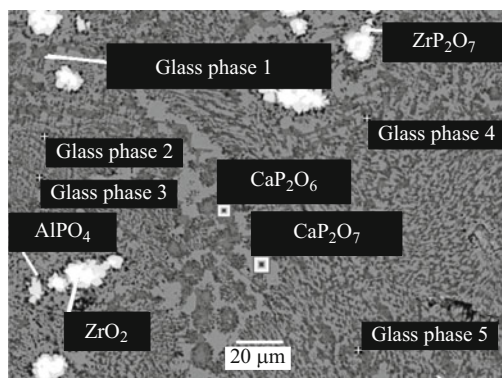


Fig. 2. Phase composition of glass ceramic material, SEM and LRSA, 900°C, 1 h.

After entering the body calcium-phosphate material (crystalline calcium phosphate, ceramic [3, 4], glass [5, 6] or pyroceramic [7 – 10]) starts to degrade. An amorphous calcium-phosphate layer with the same molar ratio $\text{CaO}/\text{P}_2\text{O}_5$ as in the initial material settles from the medium, saturated with calcium and phosphorus ions, onto the surface of the material in the implant – bone contact zone.

When silicate materials come into contact with the physiological medium in the body the alkaline cations present in them diffuse and are replaced with the hydrogen cations present in the medium, forming silica-gel on the surface. The layer becomes a matrix for the anions and cations settling from the medium, which ultimately form an amorphous calcium-phosphate layer.

Crystallization of the amorphous layers obtained in CHA — the basis of the mineral part of bone — occurs under the influence of the medium in the body in both cases.

The solubility and formation rate of amorphous layers on the surface of biomaterials are the main characteristics which make it possible to predict their behavior in the medium inside the body. The objective of the present work is to study the solubility of porous glass ceramic biomaterials based on calcium-aluminum-phosphate glass in the aqueous media in vitro and to evaluate their bioactivity in experiments in vivo.

MATERIALS AND METHODS

The chemical composition (molar content, %) of the calcium-phosphate glass ceramic material developed at the D. I. Mendeleev Russian Chemical Technology University is: 45 P_2O_5 , 50 CaO , 5 Al_2O_3 ; above 100%: 5 B_2O_3 , 5 ZrO_2 , 5 TiO_2 . Glass with this composition was made at temperature 1350 – 1400°C and formed into granules by pouring and then ground to fractions with particle sizes from 40 to 450 μm . Blanks were formed by semi-dry pressing or slip casting and sintered in the temperature interval 900 – 950°C in order to obtain porous glass ceramic materials with uniform open porosity 20 – 50% and pore size 20 – 150 μm and

channel porosity 40 – 65%, channel diameter 100 – 550 μm and pore size 20 μm .

The phase composition of the materials was determined by x-ray phase analysis (Dron-3M diffractometer, angles 8 – 25°, copper anode) and scanning electron microscopy (microprobe complex based on a Jeol JSM-6480LV scanning electron microscope combined with a system for performing x-ray spectral microanalysis and equipped with an INCA-Energy 350 energy-dispersion spectrometer and an INCA-Wave 500 wave diffraction spectrometer). The porosity and water absorption were evaluated by optical microscopy in transmitted and reflected light (“LOMO” MIN-8 and PZO microscopes) and by standard methods adopted in ceramic technology. The solubility of the materials in aqueous media (according to the mass change), pH and calcium ion concentration were determined as a function of the soaking time (20, 40, 60 and 3000 sec) at temperature 37°C.

RESULTS

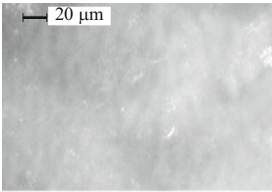
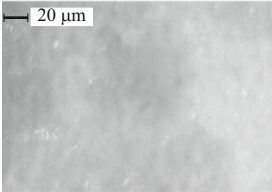
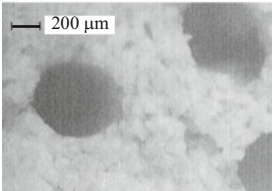
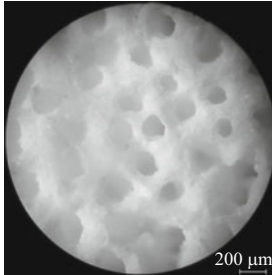
When blanks made from calcium-phosphate glass powders by semidry pressing or slip casting are sintered crystallization with formation of a multiphase glass ceramic structure and crystallinity $\geq 80\%$ occurs in the temperature range 900 – 1000°C. It consists of a residual glass phase with variable composition, crystals of calcium α - and β -pyrophosphates and titanium and zirconium pyrophosphates (Fig. 2). Calcium, titanium and zirconium phosphates are soluble in a neutral medium at low temperatures, while the phosphate residual glass phase depleted of modifying cations possesses a higher solubility than crystalline compounds and the initial calcium-aluminum-phosphate glass.

Since the chemical and phase compositions of the porous materials are identical the main factors affecting their solubility is the porosity. Several series of porous materials were synthesized for tests in aqueous media; the characteristics of these materials are presented in Table 1.

Tests performed on the materials in water at room temperature showed that water-saturation depends not so much on the magnitude of the open porosity as on the pore size and character of the pore structure. Thus, the amount of absorbed liquid is 14 – 30 wt.% for material with a uniform pore structure, 20 – 45% with channel porosity to 50%, and 10 – 17 wt.% with channel porosity 60%.

For glass ceramic materials with uniform open porosity which are obtained from powders with different particle-size fractions but the same amount of pore former, the pore sizes depend directly on the particles size of the sintered powders and constitute 20 – 150 μm . Liquid penetrates into large pores more rapidly than into small pores, as the test results show clearly. Thus, the water saturation of materials sintered from powders with grain size 40 – 80 μm (their porosity is somewhat higher) is lower than in materials sintered from larger fractions. The water absorption after the samples are boiled is essentially independent of the size of the sintered

TABLE 1. Characteristics of the Materials Used for *In Vitro* and *In Vivo* Tests

Form of material	Porosity, %	Pore size, μm	Synthesis parameters
<i>Semidry formation, isothermal heat-treatment regime</i>			
	20	20 – 100	Pressing pressure 2.5 MPa, glass powder fraction 125 – 250 μm , $T = 1000^\circ\text{C}$, 1 h
	30	60 – 150	Pore former — calcium carbonate 3 wt.%, glass powder fraction 80 – 125 μm , $T = 950^\circ\text{C}$, 1 h
	45	500 (channel) 100 – 160 (interchannel)	Pore former — graphite rods 4 wt.%, glass powder fraction 250 – 315 μm , $T = 975^\circ\text{C}$, 1 h
<i>Slip technology, non-isothermal heat-treatment regime</i>			
	60	80 – 120 (channel) 5 – 40 (interchannel)	Pore former — cotton thread 20 vol.%, glass powder fraction 40 – 80 μm , $T = 900^\circ\text{C}$, 1 h

particles and much higher than with saturation of the same samples at room temperature (Table 2).

Studies of water saturation and absorption of materials with channel pores showed the same behavior as observed for materials with uniform porosity. Water saturation of materials with channel pores obtained by semidry formation and slip casting depends on the size of the channels and pores in the interchannel barrier (Table 3). The channel size is determined by the diameter of the consumable pore agents (graphite rods in the first case and cotton threads in the second) and comprises 500 and 120 μm , respectively. The pores in the interchannel barriers are larger than in materials sintered from a larger fraction. The study showed that for materials with open porosity 53 – 54%, which are obtained using a pore agent — graphite rods, water absorption equals water saturation. For materials obtained using thread with open porosity > 50% water absorption is three times greater than water saturation.

The dissolution of materials in water at 25°C is accompanied by an increase of mass losses, decrease of pH and increase of calcium ion concentration (Fig. 3). The minimal changes in these parameters are characteristic for materials

TABLE 2. Characteristics of Porous Glass Ceramic Materials with Uniform Pore Structure and Pore Size 20 – 150 μm

Glass powder with particle size, μm	Pore former (starch) content, wt.%	Open porosity, %	Water saturation 25°C , wt.%	Water absorption during boiling, wt.%
40 – 80	3	50	14 – 16	36
125 – 250	3	47	28	32
250 – 315	3	46	30 – 31	31
40 – 80	1	30	12	15
40 – 80	3	48	19 – 21	35
40 – 80	5	31	9	15

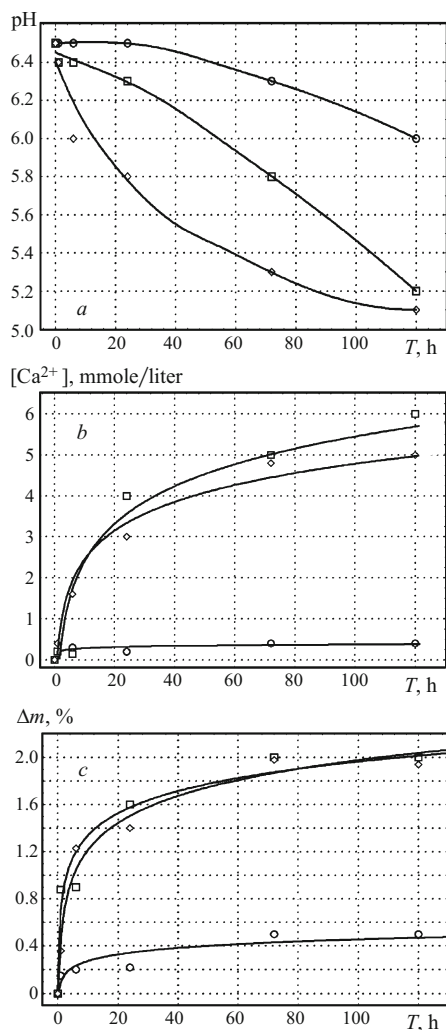


Fig. 3. Effect of the thermostating time at 25°C on the parameters of an aqueous medium: *a*) pH; *b*) calcium ion concentration, mmole/liter; *c*) sample losses, wt.%; types of materials: \circ) with uniform pore structure and open porosity 50%; \square) with channel pore structure and open porosity, 50%; \diamond) with channel pore structure and open porosity 60%.

with a uniform pore structure. For materials with channel porosity the mass losses and calcium ion concentration in the test medium grow just as rapidly, while the pH decreases to a value close to 5. Here it is evident that during long-time tests even at room temperature the intensity of the process depends on the magnitude of the open porosity.

Another test medium is an artificial physiological solution (SBF). The tests were performed at 37°C, since this temperature is close to the average temperature of the human body (Fig. 4).

The studies showed that thermostating for 360 h in a salt solution decreases the pH very little (6.3–6.4 in SBF and 4.8–5.1 in water). By the completion of thermostating the concentration of calcium ions increases to 11 mmole/liter and somewhat higher in water, which is natural at higher temperature.

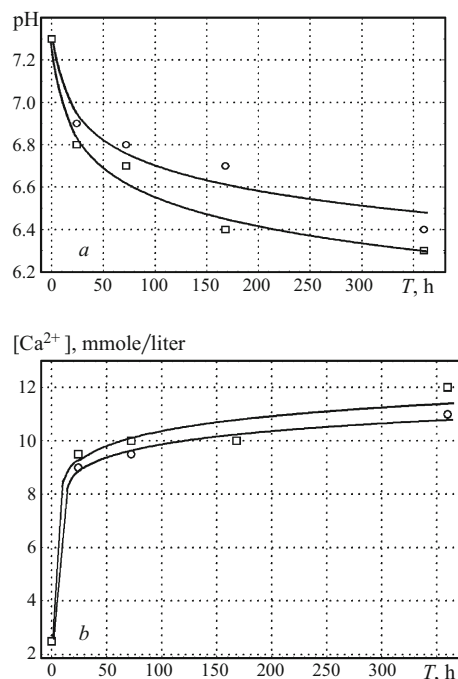


Fig. 4. Effect of the thermostating time for materials in SBF at 37°C on the parameters of the medium: *a*) pH; *b*) calcium ion concentration, mmole/liter; types of materials: \circ) with uniform pore structure and open porosity 50%; \square) with channel pore structure and open porosity 50%.

The mass losses of materials in SBF are close to zero, which seems strange when the concentration of calcium ions in solution increases. In the process a layer of x-ray amorphous white powder, less than 100 μm thick, appears on the surface.

TABLE 3. Characteristics of Glass Ceramic Materials with Channel Pore Structure

Pore agent		Open porosity, %	Water saturation at 25°C, wt. %	Water absorption during boiling, wt. %
Material	Content, wt. %			
Semidry formation with glass powder fraction 40 – 80 μm				
Graphite rods	4.2	42	22 – 29	31
	7.0	46	29 – 31	31
	8.4	46	28 – 32	32
Semidry formation with glass powder fraction 80 – 125 μm				
Graphite rods	5.6	52	37 – 40	40
	7.0	53	41 – 43	43
	8.4	54	40 – 43	43
Slip casting with glass powder fraction 40 – 80 μm				
Cotton thread	15*	39	4 – 7	27
	20*	42	7 – 9	28
	25*	45	7 – 10	30
	30*	50	8 – 11	33
	35*	65	13 – 17	39

* Content, vol. %.

CONCLUSIONS

The results show that in macroporous systems, such as the materials developed, with the same phase composition the solubility is determined by the magnitude of the open porosity and the pore size. The appearance of an amorphous surface layer during the first three days of keeping the materials in SBF essentially means that an inorganic matrix for the bone tissue starts to form. Materials with large pores and channels are preferable in order to use these systems in endoprosthesis replacement, since they are more easily permeated by aqueous physiological media. Materials with porosity greater than 60% and channel size about 120 μm can be recommended for delivering pharmaceutical preparations to the focus of disease — their slow saturation also signifies that the preparation is released into the surrounding tissue gradually, over a long period of time.

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